

CBER: BACK TO THE FUTURE

Kathryn C. Zoon, Ph.D.
WCBP 2003
San Francisco, CA
January 8, 2003

The Regulatory Pendulum

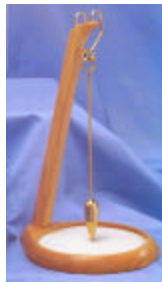
Centralization

Enforcement

Legal emphasis

Privatization

Process



Decentralization

Education

Science-based

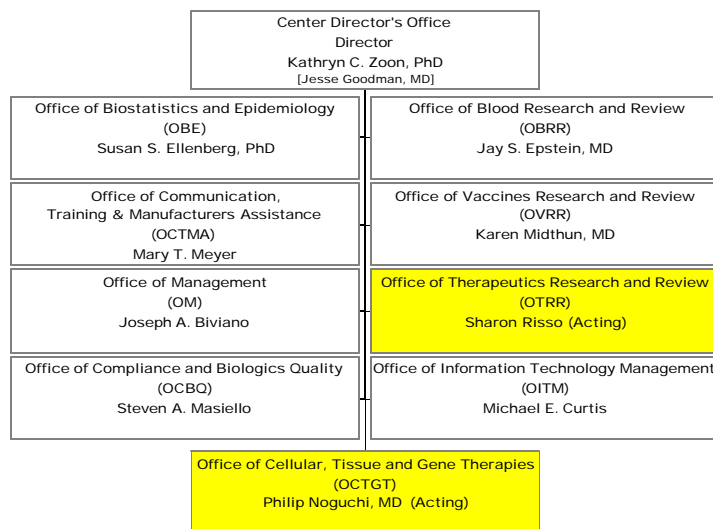
Government

Content

CBER CHALLENGES 2003

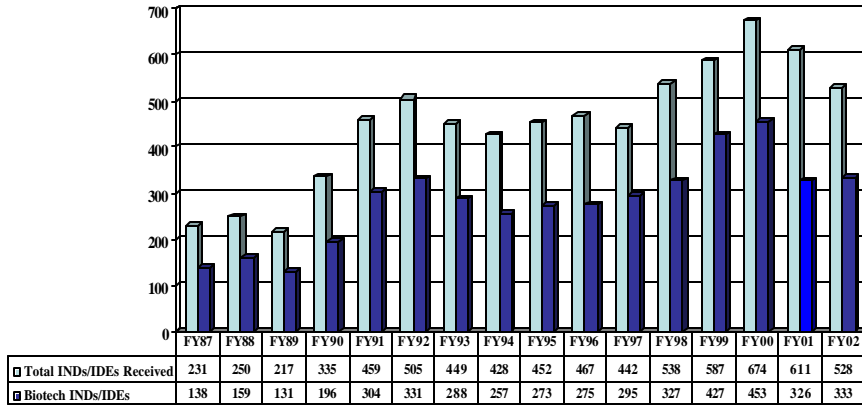
- **Organizational Changes**
- **New Performance Goals**
- **New Technologies**
- **International Harmonization**
- **E-business**
- **Counterterrorism**
- **Strong Regulatory Research Programs**

CBER Organization



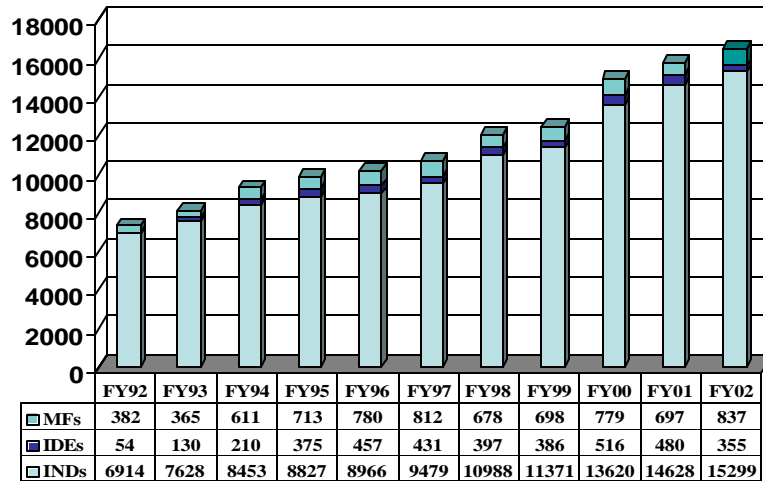
Biotech INDs/IDEs

Compared to Total
Received FY 1987 - FY 2002



(124ir)RIMS: 10/03/02

CBER IND/IDE/MF Amendments Received FY92- FY02

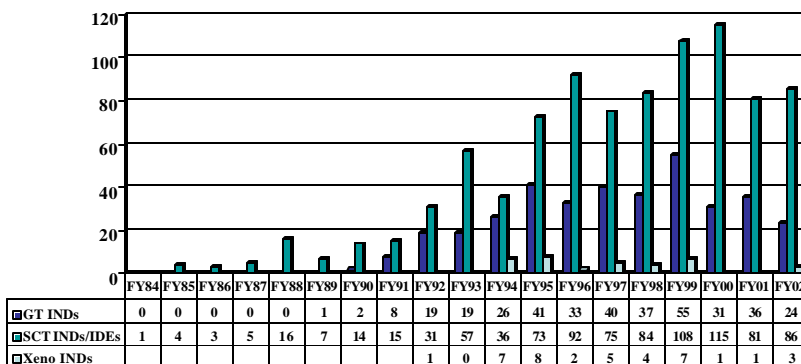


(133ir)RIMS: 10/3/02



Gene Therapy, Somatic Cell Therapy, and Xenotransplantation INDs/IDEs

Received FY 1984 - FY 2002



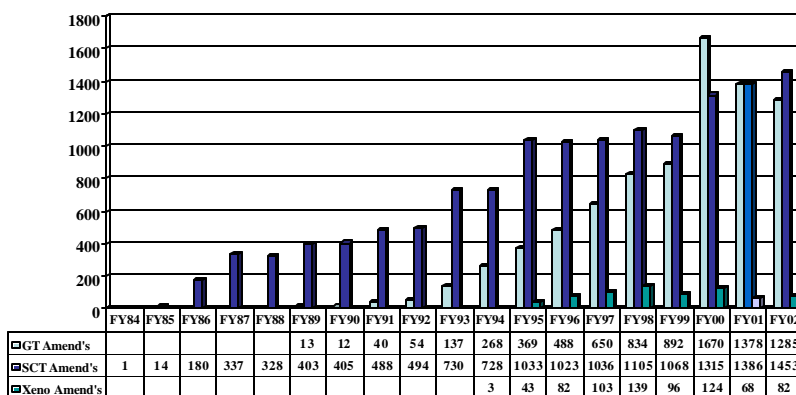
Note: A total of 7 INDs were for Xeno and GT, and are included in the counts for both.



(148ir)RIMS:10/03/02

Gene Therapy, Somatic Cell Therapy, and Xenotransplantation IND/IDE Amendments

Received FY 1984 - FY 2002



Note: A total of 317 Amendments were for INDs that are both Xeno and GT and are included in the counts for both.



(147ir)RIMS:10/03/02

CBER PRODUCTS

2003

TODAY

- Vaccines
- Allergenic Products
- Blood and Blood Products
- Blood derivatives and recombinant analogues
- Tissue, Cell and Gene Therapies
- rDNA therapeutic proteins
- Monoclonal Antibodies
- Therapeutic Vaccines
- Biologics-related devices and drugs

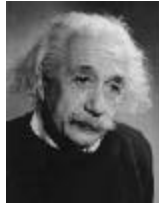
TOMORROW

- Vaccines
- Allergenic Products
- Blood and Blood Products
- Blood derivatives and recombinant analogues
- Tissue, Cell and Gene Therapies
- Therapeutic Vaccines??
- Biologics-related devices and drugs
- Some cytokines, monoclonal antibodies, and growth factors

Performance-Based Organization

- **Prescription Drug User Fee Program**
- **Medical Device User Fee Modernization Act**
- **Blood and Tissue Safety**

Performance-Based Organization



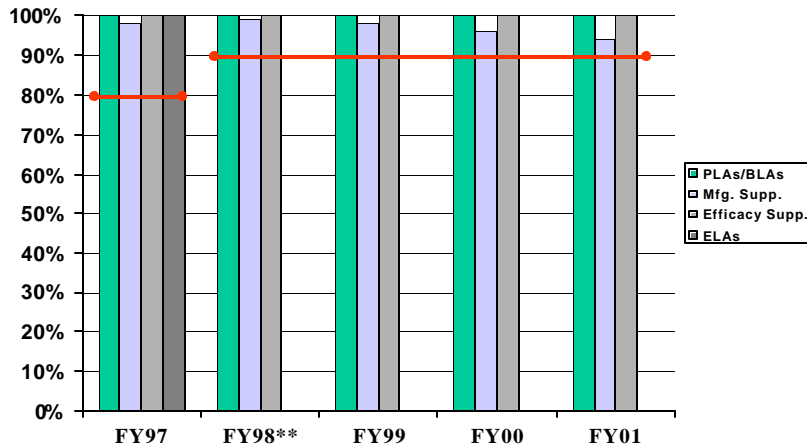
“Not everything that
counts can be
counted, and not
everything that can be
counted counts”

Albert Einstein

CBER Biologics License Application Approvals for Biotechnology Products 1981-2002

<u>Years</u>	<u>Therapeutics*</u>	<u>Vaccines</u>	<u>IVD</u>	<u>Total</u>
1981-85	0	0	23	23
1986-90	6	2	35	43
1991-95	13	0	59	72
1996-00	26	2	26	54
2000-02	11	2	5	18
<hr/>				
Total	56	6	148	210

CBER User Fee Review Performance
License Applications and Supplements
% of First Actions Within Goal*
By Cohort Fiscal Years 1997-2001



* PDUFA Performance Goals: FY97 - FY01=90% (Indicated by Red Lines)

** Beginning in FY98 ELAs were no longer included in PDUFA goals

(253bp)RIMS 12/26/02

CBER PDUFA II Procedural and Processing Goals Performance
(as of December 31, 2002)

Regulatory Meetings Management										
Fiscal Year	Goal	Meeting Requests Received	Actions Within Goal			Actions Overdue			% Completed Within Goal ¹	PDUFA Goal
			Completed	Pending	Total	Completed	Pending	Total		
FY 1999	Response	387	283	0	283	104	0	104	73%	70%
	Held	364	321	0	321	43	0	43	88%	
	Minutes	328	282	0	282	46	0	46	86%	
FY 2000	Response	312	302	0	302	10	0	10	97%	80%
	Held	294	277	0	277	14	3	17	94%	
	Minutes	251	229	0	229	19	3	22	91%	
FY 2001	Response	388	379	0	379	9	0	9	98%	90%
	Held	341	330	0	330	10	1	11	97%	
	Minutes	293	286	0	286	7	0	7	98%	
FY 2002	Response	415	401	0	401	12	2	14	97%	90%
	Held	374	360	0	360	9	5	14	96%	
	Minutes	335	317	2	319	6	10	16	95%	

¹ - of those that have reached the goal date

CBER PDUFA II Procedural and Processing Goals Performance
– cont. (as of December 31, 2002)

Special Protocol Assessment									
Fiscal Year	Protocol Review Requests Received	Actions Within Goal			Actions Overdue			% Completed Within Goal ¹	PDUFA Goal
		Completed	Pending	Total	Completed	Pending	Total		
FY 1999	0								60%
FY 2000	0								70%
FY 2001	1	1	0	1	0	0	0	100%	80%
FY 2002	4	4	0	4	0	0	0	100%	90%

Major Dispute Resolution									
Fiscal Year	Dispute Resolution Requests Received	Actions Within Goal			Actions Overdue			% Completed Within Goal ¹	PDUFA Goal
		Completed	Pending	Total	Completed	Pending	Total		
FY 1999	1	1	0	1	0	0	0	100%	70%
FY 2000	0								80%
FY 2001	2	2	0	2	0	0	0	100%	90%
FY 2002	4	4	0	4	0	0	0	100%	90%

Responses to Clinical Holds									
Fiscal Year	Responses to Clinical Holds Received	Actions Within Goal			Actions Overdue			% Completed Within Goal ¹	PDUFA Goal
		Completed	Pending	Total	Completed	Pending	Total		
FY 1998	22	18	0	18	4	0	4	82%	75%
FY 1999	77	73	0	73	4	0	4	95%	90%
FY 2000	89	87	0	87	2	0	2	98%	90%
FY 2001	125	115	0	115	10	0	10	92%	90%
FY 2002	121	118	0	118	3	0	3	98%	90%

¹ - of those that have reached the goal date

CBER Review Performance
FY 2002 Cohort of User Fee Applications

Application Types	Numbers				Percent of Actions	
	Submitted	Filed	AP	RTF, UN, or WF	Within Goal	Overdue
New Products	10	9	0	1	22%	0%
Effectiveness Supplements	11	11	2	0	45%	0%
Manufacturing Supplements	748	748	378	0	74%	1%

AP=Approved, RTF=Refuse To file, UN=Unacceptable For Filing, WF= Withdrawn Before Filing

Selected CBER Products Approved in 2002

Pegfilgrastin	• Dec infections, nonmyeloid ca
Ibritumomab	• Relapsing or refractory non Hodgkins lymphoma
Interferon beta-1a	• Relapsing multiple sclerosis
Rasburicase	• Mgt. Plasma uric acid ped. Cancer pts
Peginterferon alfa 2a	• Hepatits C
DTaP/HepB/IPV	• Combination childhood vaccine
HIV-1 PCR/ HCV-PCR	• Detection of HIV-1 and HCV in hu plasma
Adalimumab	• Some forms of severe active rheumatoid arthritis

For the CBER Record

- The number of CBER new product approvals is increasing
- CBER has demonstrated international in Biotech Product Regulation
- Despite the complexity of biotech products, review times and approval times compare favorably with those of other types of drugs
- Biological therapeutics are often available first in the USA
- Never a recall of an OTRR-approved biotech product due to safety concerns

Number of Approvals Within 12 Months

- CY 1996-2000, 14 of 22 BLAs submitted to OTRR approved within 12 months (64%)
- 13 were priority review; 10 within 12 months
- 9 were standard review; 4 approved within 12 months

Number of Cycles to Approval

- From CY 1995-2001, OTRR approved 41% of the original BLAs submitted with 1 cycle
- 19% took 3 or more cycles
- Numbers are comparable to NMEs approved during this same time period

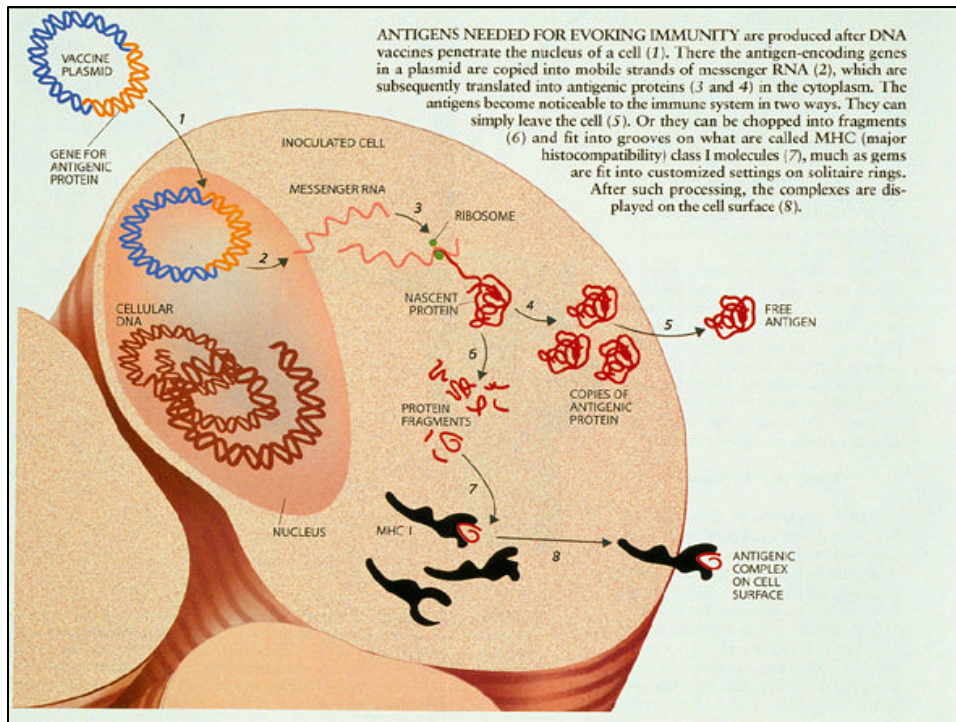
New Technologies

- New Vaccines
- Cellular and Gene Therapies
- Proteomics and Genomics
- Transgenics: Plants and Animals
- New Diagnostics for Blood and Tissue Safety

Vaccines of the 21st Century

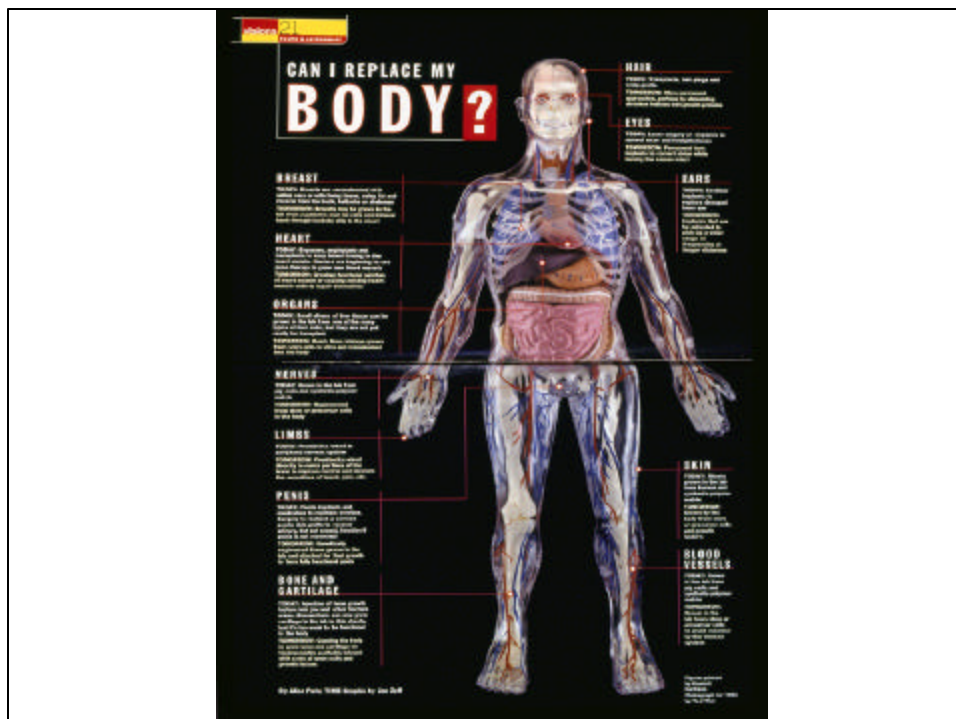
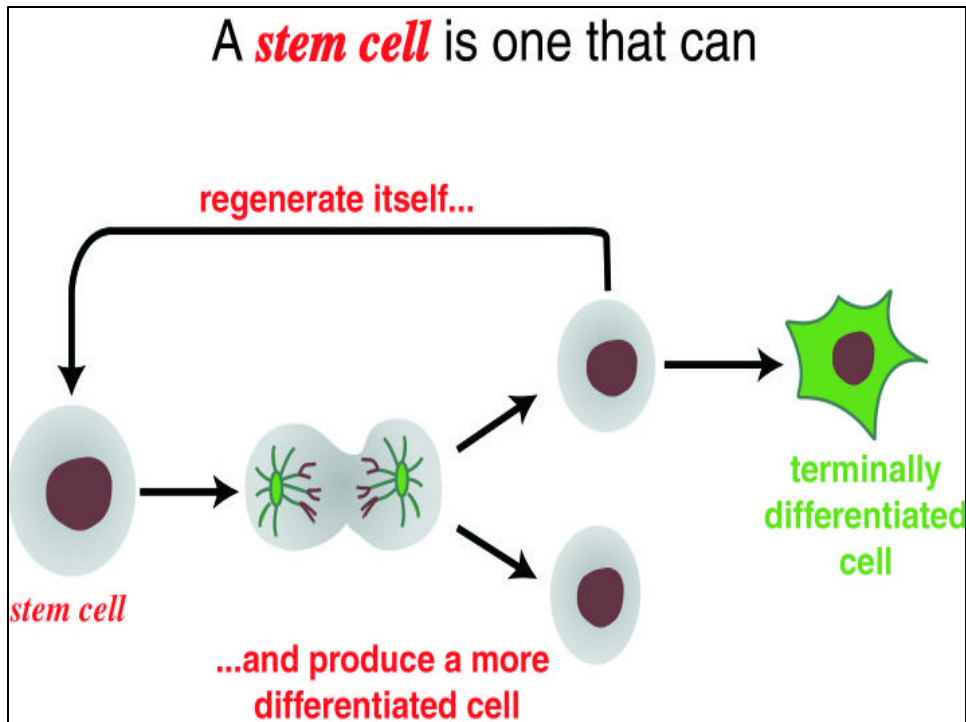
New Vaccines

- Nucleic Vaccines
- Live Attenuated Vaccines
- Combination Vaccines
- Therapeutic Vaccines



Cell and Tissue Therapies, e.g.

- Hematopoietic stem cells
- Embryonic stem cells
- Expanded lymphocytes
- Assisted reproductive technologies
- Tissue engineering
- Pancreatic islet cells
- Hepatocytes
- Cartilage
- Xenotransplantation



CBER views on Genomics and Proteomics:

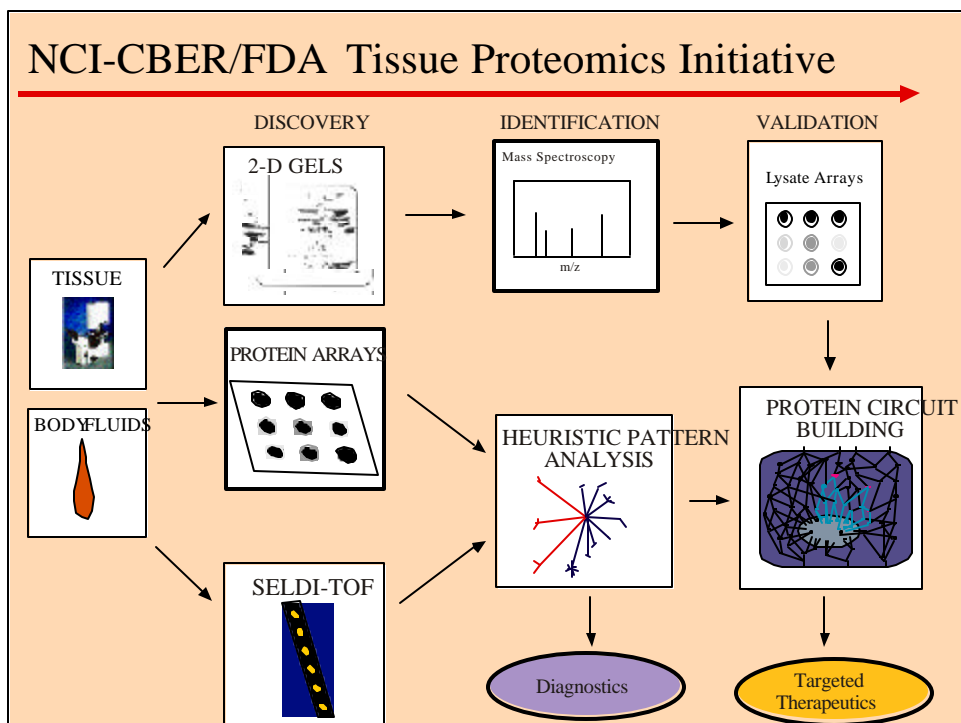
- Critical component of safe and effective drug development
- Basis for new drug discovery, biomarkers and surrogate endpoints for toxicity and efficacy monitoring
- Means to detect and assess chemical and biological terrorist agents

Regulatory Impact

- Vaccine assessment/potency
- Surrogate endpoints- efficacy/toxicity
- Quality control/quality assurance for product production
- New Bioassays
- Biomarkers for early detection
- Toxicity detection and prediction

Regulatory Impact (cont.)

- Discovery of new therapeutics targets
- Risk of disease recurrence
- Patient-tailored therapy. Prospective selection
- New paradigm in disease classification/characterization
- Proteomic-based epidemiology



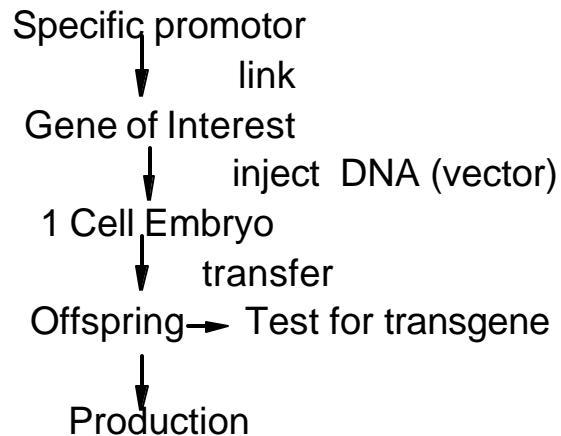
Transgenics

Transgenic Plant and Animal Products

- Vaccines
- Monoclonal Antibodies
- Therapeutic Proteins



Transgenic Animal Biological Product



Blood Safety in the 21st Century

- New Blood Screening Tests, e.g. West Nile Virus
- Pathogen Inactivation
- Blood Substitutes

International Harmonization

- International Conference on Harmonisation: Q, S, E and M topics
- World Health Organizations
- US FDA and EU bilateral
- National Institute for Biological Standards and Controls (NIBSC), United Kingdom
- Interactions with Individual Countries, e.g. Mexico, Canada, Switzerland

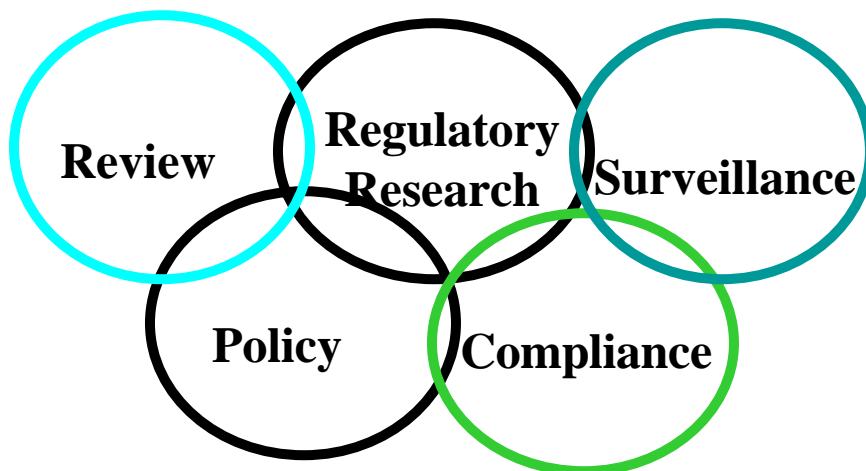
CBER e-Business

- CBER is the first Center to accept fully electronic regulatory documents with digital signatures and automated submission and processing via ESM
- The EDR, ESM, and e-Routing are a complete, robust set of review tools to meet reviewer needs, developed in conjunction with the reviewer community
- CBER's electronic submission infrastructure and applications may form the core of an overall FDA electronic submission toolset
- The CBER Electronic Submissions program is robust and has made great strides since its inception in 1996



COUNTER- BIOTERRORISM

Regulation of Biological Products Based on Sound Science, Law, and Public Health Impact



CBER Future

***Destiny is not a matter of
chance; it is a matter of
choice. It is not
something to be waited
for; but rather
something to be
achieved.***

***William Jennings
Bryan***

***FDA regulation should be
based on good science
and good sense***

K. Zoon